## II. REMARKS

**Formal Matters**

Claims 1, 3, and 5-43 are pending after entry of the amendments set forth herein.

Claims 1-8 and 13-21 were examined and were rejected. The Office Action stated that claims 9-12 were withdrawn from consideration.

Claims 1, 3, 6-8, 13-16, 18, 20, and 21 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim. Support for the amendments to claims 1, 3, 6-8, 13-16, 18, 20, and 21 is found in the claims as originally filed, and throughout the specification, in particular at the following exemplary locations: paragraph 0037; and the Examples. Accordingly, no new matter is added by these amendments.

Claims 2 and 4 are canceled without prejudice to renewal, without intent to acquiesce to any rejection, and without intent to surrender any subject matter encompassed by the canceled claims. Applicants expressly reserve the right to pursue any canceled subject matter in one or more continuation and/or divisional applications.

Claims 31-43 are added. Support for new claims 31-43 is found in the claims as originally filed, and throughout the specification, including the following exemplary locations: claim 31: paragraph 0037; claims 32 and 33: paragraph 0038; claims 34 and 35: paragraph 0036; claim 36: paragraphs 0012, 0055, and 0063; claim 37: paragraph 0047; claim 38: paragraph 0048; claim 39: Example 1 and paragraph 0075; claims 40-43: paragraph 0075. Accordingly, no new matter is added by these new claims.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Restriction requirement

The instant Office Action stated that claims 1-21 are pending, and claims 9-12 are withdrawn from consideration. However, as of the mailing date of the instant Office Action, claims 1-30 were pending in this application.

The Restriction Requirement mailed June 4, 2004 indicated that claims 1-30 were pending. The response, filed July 1, 2004, to the Restriction Requirement elected Group I (claims 1-8 and 13-21). No claims were canceled. Accordingly, as of the mailing date of the instant Office Action, claims 1-30

were pending. Applicants presume that the Office Action intended to indicate that claims 9-12 and 22-30 are withdrawn from consideration.

Rejections under 112, first paragraph

Claims 1-8 and 13-21 were rejected under 35 U.S.C.§112, first paragraph, as allegedly lacking enablement. Claims 1-8 and 13-21 were rejected under 35 U.S.C.§112, first paragraph, as allegedly failing to comply with the written description requirement.

Enablement

The Office Action stated that the specification does not reasonably provide enablement for:

1) any transgenic non-human mammal other than mouse or goat;
2) comprising a transgene encoding any fatty acid desaturase;
3) wherein said transgene comprises a coding sequence for a stearoyl CoA desaturase operably linked to any animal tissue specific promoter other than mammary gland tissue promoter;
4) a method for producing the transgenic non-human animal comprising introducing a desaturase transgene into a somatic cell, forming a genetically modified somatic cell comprising a genetically modified nucleus and transferring the genetically modified somatic cell into a single-celled embryo, and transferring the genetically modified embryo into a recipient female, wherein the genetically modified embryo develops into a transgenic animal; and
5) a method for producing a food product comprising harvesting or processing a food product from the transgenic non-human animal.

Applicants respectfully traverse the rejection.

*Transgenic non-human animals*

The Office Action stated that the specification does not reasonably provide enablement for any transgenic non-human mammal other than mouse or goat. The Office Action stated that the specification does not teach a transgenic non-human animal of any species other than mouse or goat. Applicants respectfully traverse the rejection.

Applicants have provide ample guidance which, when combined with the knowledge and skill in the art, provides an enabling disclosure for how to make and use a transgenic non-human animal as

claimed. The specification provides ample guidance as to how to make a variety of transgenic non-human animals. Specification, paragraphs 0056-0064. As the Office Action acknowledged, the specification provides working examples of two different non-human transgenic animals – mouse and goat - comprising a transgene encoding a fatty acid desaturase, e.g., stearoyl CoA desaturase (SCD). Specification, Example 1. Furthermore, the specification provides a detailed example of how to generate a transgenic pig comprising a transgene encoding a fatty acid desaturase, e.g., SCD. Furthermore, methods of making various other transgenic non-human animals, such as transgenic chickens, and transgenic cows, were well known in the art, as set forth in the specification. Specification, paragraphs 0063 and 0064. Accordingly, the instant specification provides ample support as to how to make and use a transgenic non-human animal as claimed.

Furthermore, the U.S. Patent & Trademark Office (U.S. PTO) has issued several patents containing claims that recite "a transgenic non-human mammal," where such patents provide no more, and in many instances provide less, disclosure as to how to make and use the transgenic non-human mammals being claimed. A list of examples of patents issued by the U.S. PTO follows.

U.S. Patent No. 6,518,482 issued with claims reciting "A non-human transgenic mammal." U.S. Patent No. 6,518,482 provides a working example of a transgenic mouse; and does not provide any examples, working or prophetic, of any transgenic non-human mammal other than mouse.

U.S. Patent No. 6,743,966 issued with claims reciting "A transgenic non-human mammal." U.S. Patent No. 6,743,966 provides a working example of a transgenic mouse; and does not provide any examples, working or prophetic, of any transgenic non-human mammal other than mouse.

U.S. Patent No. 6,268,545 issued with claims reciting "A transgenic non-human transgenic mammal." U.S. Patent No. 6,268,545 provides a working example of a transgenic mouse; and does not provide any examples, working or prophetic, of any transgenic non-human mammal other than mouse.

U.S. Patent No. 6,262,336 issued with claims reciting "A transgenic non-human mammal." U.S. Patent No. 6,262,336 provides a working example of a transgenic mouse and a transgenic pig; and does not provide any examples, working or prophetic, of any transgenic non-human mammal other than mouse and pig.

U.S. Patent No. 6,222,094 issued with claims reciting "A transgenic non-human mammal." U.S. Patent No. 6,222,094 provides examples of a transgenic mouse and a transgenic cow; and does not provide any examples, working or prophetic, of any transgenic non-human mammal other than mouse and cow.

U.S. Patent No. 6,204,431 issued with claims reciting "A transgenic non-human mammal." U.S. Patent No. 6,204,431 provides a working example of a transgenic mouse and a transgenic rabbit; and does not provide any examples, working or prophetic, of any transgenic non-human mammal other than mouse and rabbit.

U.S. Patent No. 6,025,540 issued with claims reciting "A transgenic non-human mammal." U.S. Patent No. 6,025,540 provides a working example of a transgenic mouse and a transgenic calf; and a prophetic example of a transgenic rabbit; and does not provide any example, working or prophetic of any transgenic mammals other than mouse, cow, and rabbit.

*Fatty acid desaturase genes*

The Office Action stated that the specification does not teach any transgenic non-human animal comprising a transgene encoding any fatty acid desaturase other than stearoyl CoA desaturase (SCD). Applicants respectfully disagree.

However, the specification provides ample description for how to make and use a transgenic non-human mammal comprising a desaturase-encoding transgene. The specification provides ample guidance as to how to make a variety of transgenic non-human animals. Specification, paragraphs 0056-0064. The specification provides sources for nucleotide sequences encoding various desaturase proteins, which nucleotide sequences were well known in the art as of the priority date of the instant patent application. Specification, paragraph 0066. The specification provides working examples of transgenic non-human mammals comprising a transgene encoding SCD. Using the ample guidance provided in the specification, together with the knowledge and skill level in the art, those of ordinary skill in the art could make a transgenic non-human animal comprising a transgene encoding any desaturase.

*Tissue-specific promoters*

The Office Action stated that the specification does not reasonably provide enablement for a transgenic non-human animal, where the transgene comprising a coding sequence for a SCD operably linked to any tissue-specific promoter other than mammary gland tissue promoter. Applicants respectfully disagree.

The instant specification provides ample description of various tissue-specific promoters, many of which were known in the art as of the priority date of the instant application, and were known to direct expression in a tissue-specific manner. Specification, paragraphs 0074-0078. Accordingly, the instant specification provides ample guidance for various tissue-specific promoters.

The Office Action acknowledged that the specification provides guidance as to how to make a transgenic mouse comprising a transgene encoding SCD operably linked to an epithelial tissue specific promoter. The Office Action stated that the specification does not teach how to distinguish the transgenic mouse with a mouse comprising a transgene operably linked to a different tissue specific promoter. However, the specification states that a tissue-specific promoter provides for preferential expression in a given tissue. Specification, paragraph 0074. The specification lists a number of epithelial cell-specific promoters, each of which was well known in the art. Specification, paragraph 0078. As of the priority date of the instant application, those skilled in the art were well aware of techniques for determining whether a given promoter controlled expression in a tissue-specific manner. For example, the references listed in paragraph 0078 provide evidence that those skilled in the art could readily determine whether a transgene was being expressed preferentially in intestinal epithelial cells. Accordingly, the specification provides ample guidance as to how to make a transgenic non-human animal comprising a desaturase-encoding transgene, where the nucleotide sequence encoding the desaturase is operably linked to a tissue-specific promoter.

*Method for producing a non-human transgenic animal*

The Office Action stated that the instant specification does not reasonably provide enablement for a method of producing a transgenic non-human animal, comprising introducing an SCD transgene into a somatic cell, forming a genetically modified somatic cell, transferring the genetically modified nucleus of the somatic cell into a single-celled embryo, generating a genetically modified embryo, and transferring said embryo into a recipient female, where the embryo develops into a transgenic animal in the female. Applicants respectfully disagree.

As of the priority date of the instant application, those skilled in the art were aware of methods of making transgenic non-human animals using nuclear transfer; and the specification provides references to such methods. Specification, paragraphs 0059-0061. Accordingly, the specification provides ample guidance as to how to make a transgenic non-human animal as claimed, using nuclear transfer of a genetically modified somatic cell.

Written description

The Office Action stated that: 1) the instant specification does not disclose the physical structure, function, and utility of a sufficient number of transgenic non-human animals; 2) the sequence of the rat gene disclosed in the specification would not be representative of the entire genus; and there is not a

description of the phenotype of any mammal other than mouse and goat; and 3) the specification does not disclose the physical structure, function, and utility of a transgenic non-human animal comprising a fatty acid desaturase operably linked to any tissue-specific promoter. Applicants respectfully traverse the rejection.

The written description requirement of 35 U.S.C.§112, first paragraph, requires that the invention be described in such a way that those skilled in the art would recognize that the applicant had, as of the priority date of the application, possession of the invention. It is Applicants' position that the written description requirement has been met.

1) Transgenic non-human animals

As the Office Action acknowledged, Applicants provide working examples of transgenic non-human animals of two different species: mouse and goat. The specification provides ample description of a subject transgenic non-human animal. For example, the specification states that the level of saturated fatty acids (SFA) in a subject transgenic non-human animal is lower than the level of SFA in a control animal; that the level of monounsaturated fatty acids (MUFA) in a subject transgenic non-human animal is higher than the level of MUFA in a control animal; and that the level of polyunsaturated fatty acids (PUFA) in a subject transgenic non-human animal is higher than the level of PUFA in a control animal. Specification, paragraphs 0036-0038. Those skilled in the art would recognize that, by showing working examples of transgenic non-human animals of two different species, along with the knowledge of those in the art, Applicants had possession of the invention as claimed. Accordingly, the specification provides adequate written description of a transgenic non-human animal as claimed.

2) Fatty acid desaturase transgenes

The Office Action stated that "the genus would encompass fatty acid desaturase genes from any animal which again would have different nucleic acid an amino acid structure and the sequence of rat gene disclosed in the specification would not be representative of the entire species." Office Action, page 13. However, as noted above, the specification discloses publicly available sources of nucleotide sequences encoding a variety of fatty acid desaturases, as well as a variety of stearoyl CoA desaturases. Accordingly, those skilled in the art would recognize that Applicants had possession of the invention as claimed. Accordingly, the specification provides adequate written description of fatty acid desaturase transgenes.

3) Tissue-specific promoters

The Office Action stated that "the working example provided in the specification does not allow a skilled artisan to envision the specific structure, function and utility of any transgenic non-human animal comprising any fatty acid desaturase linked to any tissue specific promoter." Office Action, page 15. However, the instant specification provides working examples for both transgenic mice and transgenic goats, where the desaturase-encoding nucleotide sequence of the transgene is operably linked to a mammary-specific promoter, and where the fatty acid composition of the milk produced by the transgenic animals was altered. Specification, Example 1. The instant specification also provides a detailed description of how to make a transgenic non-human animal, where the desaturase-encoding nucleotide sequence of the transgene is operably linked to an intestinal epithelial cell-specific promoter. Specification, Example 2. In Example 2, the sequence of primers that amplify an intestinal epithelial cell-specific promoter are given. Thus, the specification provides ample description which, together with the knowledge in the art, would lead a person skilled in the art to recognize that Applicants had, as of the priority date of the instant application, possession of the claimed invention.

Conclusion as to the rejections under 35 U.S.C.§112, first paragraph

Applicants submit that the rejection of the claims discussed above under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejections under 35 U.S.C.§102

Claims 1, 2, 5, 13, and 14 were rejected under 35 U.S.C.§102(b) as allegedly anticipated by Miyake et al. ((2001) *J. Biol. Chem.* 276:23304-23311; "Miyake"). Claims 1-5, 13-15, 20, and 21 were rejected under 35 U.S.C.§102(e) as allegedly anticipated by Knutzon et al. (U.S. Patent No. 5,968,809; "Knutzon").

Claims 1, 2, 5, 13, and 14 over Miyake

The Office Action stated that Miyake teaches a transgenic mouse comprising a chromosomally integrated transgene encoding 7α-hydroxylase, a fatty acid desaturase. Applicants respectfully traverse the rejection.

Claim 2 is canceled without prejudice to renewal, thereby rendering this rejection of claim 2 moot.

The enzyme discussed in Miyake, cholesterol 7α-hydroxylase, is not a fatty acid desaturase. Accordingly, Miyake cannot anticipate claims 1, 5, 13, and 14.

Claims 1-5, 13-15, 20, and 21 over Knutzon

The Office Action stated that Knutzon teaches transgenic non-human animals comprising a transgene encoding a fatty acid desaturase. Applicants respectfully traverse the rejection.

Claims 2 and 4 are canceled without prejudice to renewal, thereby rendering this rejection of claims 2 and 4 moot.

Claim 1 as amended recites a transgenic non-human mammal comprising a transgene comprising a nucleotide sequence encoding a fatty acid desaturase, wherein a tissue of said mammal comprises a level of MUFA that is at least 5% higher than the level of MUFA in the same tissue of a non-transgenic mammal of the same species. Knutzon discusses transgenic animals comprising a desaturase gene, where the level of specific PUFAs is altered. Knutzon neither discloses nor suggests a transgenic non-human animal comprising a tissue that comprises a higher level of MUFA than a control animal. Thus, Knutzon neither discloses nor suggests a transgenic non-human mammal as recited in claim 1 as amended. Accordingly, Knutzon cannot anticipate claim 1.

Knutzon therefore cannot anticipate claims 3, 5, and 6-8, which depend from claim 1. Knutzon cannot anticipate claims 13 and 18, which, as amended, recite a method for producing the mammal of claim 1. Claims 14-17, which depend from claim 13, and claim 19, which depends from claim 18, are therefore also not anticipated by Knutzon. Claims 20 and 21 recite a method of producing a food product, involving harvesting (claim 20) or processing (claim 21) a food product from a transgenic non-human mammal of claim 1, are similarly not anticipated by Knutzon.

Conclusion as to the rejections under 35 U.S.C.§102

Applicants submit that the rejections of the claims discussed under 35 U.S.C. §102(b) and §102(e) have been adequately addressed in view of the remarks set forth above. The Examiner is thus

respectfully requested to withdraw the rejections.

Rejection under 35 U.S.C.§103(a)

Claims 1-8, 13-17, 20, and 21 were rejected under 35 U.S.C.§103(a) as allegedly unpatentable over Knutzon in view of Ward ((1997) *Biochem. Soc. Trans.* 25(S673):145; "Ward").

The Office Action stated that: (1) Knutzon teaches transgenic non-human animals comprising a transgene encoding a fatty acid desaturase such that the animals express increased levels of desaturase; and (2) Ward teaches a method for increasing the proportion of monounsaturated fatty acids in ruminant carcass by increasing the proportion of oleic acid in ovine tissue by manipulating the expression of the enzyme SCD. The Office Action stated that it would have been obvious to modify the method of Knutzon to generate transgenic non-human animals comprising a transgene encoding a fatty acid desaturase for the production of food products from the animals using a cloning method with the teachings of Ward by expressing SCD in the transgenic non-human animals. Applicants respectfully traverse the rejection.

As noted above, claim 1 as amended recites a transgenic non-human mammal comprising a transgene comprising a nucleotide sequence encoding a fatty acid desaturase, wherein a tissue of said mammal comprises a level of MUFA that is at least 5% higher than the level of MUFA in the same tissue of a non-transgenic mammal of the same species. As noted above, Knutzon neither discloses nor suggests a transgenic non-human animal comprising a tissue that comprises a higher level of MUFA than a control animal. Furthermore, Ward neither discloses nor suggests altering a level of MUFA in an animal. Therefore, it would not have been obvious, based on Knutzon, alone or in combination with Ward, that a transgenic non-human mammal comprising a fatty acid desaturase-encoding transgene would exhibit a higher level of MUFA in a tissue than a control animal. Accordingly, Knutzon, alone or in combination with Ward, cannot render the instant invention as claimed obvious.

Applicants submit that the rejection of claims 1-8, 13-17, 20, and 21 under 35 U.S.C. 35 U.S.C.§103(a) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

## III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCDV-286.

Respectfully submitted,

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Date: Nov. 17 2004

By: _____

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